NONTECHNICAL ABSTRACT

Gaucher disease causes fat to collect in bone marrow-derived cells called macrophages. Fat collects there because of an abnormality in an enzyme called glucocerebrosidase. Gaucher disease results in many health problems. Current treatment for this disease involves repeated intravenous treatment with normal enzyme. This treatment is called enzyme replacement therapy. Another treatment for Gaucher disease is bone marrow transplantation. Bone marrow transplantation involves destroying a person's bone marrow with drugs and irradiation and replacing it with someone else's bone marrow. This treatment has many risks but can cure the patient for the rest of their life. It would be good to be able to treat people with Gaucher disease with a treatment like bone marrow transplant but without the risks connected with destroying bone marrow cells and using someone else's bone marrow. Either some blood or bone marrow will be obtained. A special type of cell (stem cell) that makes all the other cells in both the blood and bone marrow including macrophages will be isolated in the laboratory. These cells will be isolated in the laboratory and used for "gene therapy". New genetic material will be put into these special stem cell using a specially modified virus called a murine retrovirus vector. The murine retrovirus has been altered so it can deliver new genetic material to a cell but not cause an infection. The new genetic material inserted into your cells using the retrovirus vector will serve as a blueprint to allow the cells to make the enzyme that was abnormal. After putting the new genetic material into the cells, these cells will be put back into the patient by needle injection into a blood vessel. This will be done without first destroying the patient's bone marrow cells. If bone marrow cells are used to obtain the stem cells, only one treatment will be done. If blood is treated, four treatments every 2 - 4 months will be done. The patients will be watched for any unexpected harmful side effects that may result from this therapy. Samples of blood and marrow cells will be taken periodically to measure the number of cells that contain the new genetic material. If enough cells contain the new genetic material, the amount of enzyme being produced will be measured. It is hoped that this study will provide doctors with more information which might permit them to develop a safe and effective gene therapy for persons with Gaucher disease.